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Original Article

The Role of Botulinum Toxin in Dry Eye Disease and Meibomian Gland Dysfunction Associated with Hemifacial Spasm

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Abstract

Objectives: To investigate the signs and symptoms of dry eye disease (DED) in patients with hemifacial spasm (HFS) through the evaluation of ocular surface measurements and meibomian gland function, and to assess the effects of botulinum toxin type A (BTX-A) injection on ocular surface health.

Methods: This prospective study included patients with unilateral HFS who underwent BTX-A injection as treatment. Eyes on the same side as the spasm were defined as the HFS group, whereas the contralateral, unaffected eyes were used as controls. Ocular surface assessments included the ocular surface disease ındex (OSDI) score, Schirmer's I test, tear break-up time (TBUT), corneal surface staining, eyelid margin abnormalities, and meibomian gland function. All evaluations were repeated at 1, 3, and 6 months following BTX-A injection.

Results: Compared to the control group, the HFS group demonstrated significantly higher OSDI scores, corneal surface staining, eyelid margin abnormalities, meibomian gland expression scores, meibography scores, and meibomian gland loss, whereas TBUT and Schirmer's I test values were significantly lower ($p<0.05$). A significant correlation was observed between the severity of HFS and ocular surface dysfunction, including meibomian gland dysfunction (MGD) ($p<0.05$). Following BTX-A injection, ocular surface parameters showed significant improvement at 1 month ($p<0.05$) and 3 months ($p<0.05$) compared to pre-injection values.

Conclusion: We found an association between HFS and DED, which was correlated with the severity of HFS. In addition, BTX-A injection led to a temporary improvement in dry eye signs and symptoms, including MGD.

Keywords: Botulinum toxin, dry eye, hemifacial spasm, meibomian gland, ocular surface

Introduction

Hemifacial spasm (HFS) refers to a chronic condition involving unilateral, involuntary facial muscle contractions due to irritation or compression of the facial nerve. Although HFS is primarily known as a motor disorder, emerging evidence suggests a significant association with ocular surface dysfunction. Patients with HFS frequently report symptoms suggestive of dry eye disease (DED), such as irritation, tearing, and eye discomfort, likely due to irregular blinking patterns and persistent orbicularis oculi muscle hyperactivity (1).

Previous research on ocular surface alterations in movement disorders has primarily focused on blepharospasm,

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which shares similar clinical features with HFS, including increased blink frequency and forceful eyelid closure (2,3). However, data specific to HFS remain limited (4,5). In particular, the role of meibomian gland dysfunction (MGD) in the pathogenesis of DED among patients with HFS remains poorly understood (4,5).

Botulinum toxin type A (BTX-A) is the mainstay treatment for HFS, offering temporary relief from muscle spasms by inhibiting acetylcholine release at neuromuscular junctions (1). While its efficacy in reducing motor symptoms is well documented, evidence regarding its effects on the ocular surface and meibomian gland function has yielded inconsistent results (3,6,7).

This research was designed to provide a comprehensive evaluation of DED among HFS patients, incorporating both patient-reported outcomes (ocular surface disease index (OSDI)) and clinical findings (tear break-up time (TBUT), Schirmer's I test, corneal staining, and meibomian gland assessment. Furthermore, we investigated the short- and midterm effects of periocular BTX-A injections on these parameters at 1-, 3-, and 6-month follow-up visits. By comparing findings from affected and contralateral eyes, this study also sought to clarify the localized impact of HFS on ocular surface homeostasis.

Methods

This prospective, cross-sectional observational study was carried out in the ophthalmology department of Dokuz Eylul University Hospital and included patients diagnosed with unilateral HFS. HFS was diagnosed based on standard criteria and confirmed by a neurology specialist (8). Exclusion criteria included the presence of ocular surface diseases other than DED, neurologic disorders other than HFS, eyelid malposition, punctal occlusion, glaucoma, contact lens wear, systemic comorbidities, prior ocular surgeries or trauma, medication use affecting tear production, and refractive errors >±4.00 diopters. The eye on the same side as the HFS was designated as the affected (homolateral) eye, whereas the non-affected (contralateral) eye served as an internal control. The study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Dokuz Eylul University (approval number: 2024/08-19). Informed consent was obtained in writing from all participants before study enrollment.

Demographic and clinical data were recorded for all patients. HFS severity was graded on a 4-point scale (0–4) based on the rating system established by Lee et al. (9) (Table 1) A single examiner performed a standardized ophthalmologic evaluation on all subjects, including both the HFS-affected and contralateral eyes, following completion of the OSDI questionnaire. The assessment protocol included Schirmer's I test, TBUT, corneal surface staining, eyelid margin grading, meibomian gland expression evaluation, and imaging with infrared meibography. Data from both eyes of each participant were included in the analysis. OSDI is a widely used, validated questionnaire comprising 12 items that assess the frequency and severity of symptoms associated with DED (10). Each item is scored on a scale from 0 (none of the time) to 4 (all of the time). The total score is determined by the following equation: (Sum of scores for all answered questions × 100)/(total number of questions answered × 4), with higher scores indicating more severe symptoms. Schirmer's I test was performed under non-anesthetized conditions using a standardized strip positioned at the outer one-third of the lower eyelid to measure tear production. The strip remained in place for 5 min, and the length of the wetted area (in millimeters) was recorded. TBUT was measured after using a minimally moistened fluorescein strip after instilling fluorescein dye into the conjunctival sac. After several blinks to evenly disperse the dye, the duration between the last complete blink and the first visible corneal dry spot was measured using cobalt blue illumination. Corneal fluorescein staining was used to evaluate superficial punctate keratopathy (11). The cornea was divided into five regions, each graded on a scale from 0 to 3, where 0 indicated no staining, 1 represented punctate staining, 2 denoted linear or ball staining, and 3 corresponded to coalesced staining. Eyelid margin abnormalities were graded on a 0–4 scale based on specific features, including lid margin irregularity, plugging of the meibomian gland orifices, vascular engorgement, and mucocutaneous junction displacement (12). Digital pressure was applied to the nasal and central regions of both

Table 1. Grading system for hemifacial spasm

Grade	Detailed description
1	Localized spasm around the periocular area
2	Involuntary movement spreads to other parts of the ipsilateral face and affects other muscle groups: The orbicularis oris, zygomaticus, frontalis, and platysma muscles
3	Interference with vision because of frequent tonic spasms
4	Disfiguring asymmetry: Continuous contraction of the orbicularis oculi muscles affects the opening of the eye

the upper and lower eyelids to evaluate meibomian gland expression. Expression quality was graded as follows: Grade 0 indicated clear meibum easily expressed, Grade 1 indicated cloudy meibum expressed with mild pressure, Grade 2 referred to cloudy meibum requiring moderate pressure, and Grade 3 indicated no expression despite firm pressure (13). Meibomian gland loss was assessed through infrared meibography and calculated as the percentage of gland dropout relative to the total area of the tarsal plate (14). Gland loss was scored using a five-grade meiboscore system: Grade 0 represented no gland loss, Grade 1 indicated <25% loss, Grade 2 indicated 25–50% loss, Grade 3 indicated 50–75% loss, and Grade 4 indicated more than 75% gland loss. The overall meiboscore was obtained by adding the individual scores of the upper and lower eyelids.

DED was diagnosed by the DEWS II guidelines, which require an OSDI score of ≥13 and at least one abnormal clinical test result, including Schirmer's I test (≤5 mm), positive corneal staining, or TBUT <10 s.(15) Patients with HFS were treated with onabotulinumtoxin A (100U, Botox, Allergan, Irvine, CA, USA) injections prepared and administered by a single clinician (Fig. 1). Each vial was reconstituted using 2 mL of preservative-free sterile saline, which produced a final concentration of 5 units/0.1 mL. The injections were performed using a 30-gauge needle at four sites in the medial and lateral pretarsal orbicularis oculi muscle and into the corrugator and procerus muscles between the eyebrows. An additional injection targeted the zygomaticus major muscle and was administered approximately 1–2 cm below the zygomatic arch along an anatomical line from the zygomatic bone to the oral commissure. A standardized total dose of 20 units of onabotulinumtoxinA was administered to the affected side in all patients. The dose was distributed as follows: 2.5 units were injected into both the medial and lateral portions of the pretarsal orbicularis oculi (totaling 5 units per eye for the periocular region), 5 units into the corrugator muscle, 5 units into the procerus muscle, and 5 units into the zygomaticus major muscle. This dosing regimen was consistent for all study participants and was not adjusted based on individual patient factors. All patients underwent ophthalmic examinations at baseline and 1, 3, and 6 months following BTX-A injections. No topical or systemic treatments for DED were administered to any patients with HFS throughout the study period.

Data analysis was performed using the Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation, and categorical variables were reported as frequencies and percentages. The Shapiro–Wilk test was applied to assess the normality of the data distribution. Independent samples t-tests were utilized for comparing continuous variables between different groups, and paired samples t-tests were conducted for within-group analyses. Chi-square tests were conducted for comparisons involving categorical data. Pearson's correlation coefficient was applied to quantify associations between continuous variables. Statistical significance was defined as a $p<0.05$. Post hoc power analysis performed with G*Power (v3.1.9.2) indicated that the study had more than 80% power to detect significant effects at the 0.05 alpha level.

Results

In this study, the 27 eyes affected by HFS were included in the HFS group, and the contralateral unaffected eyes of the same patients were used as the control group. Sixteen patients were female, 11 were male, and the mean age was 62.1±10.2 years. DED was diagnosed in 17 (44.4%) patients with HFS. The clinical characteristics and ocular surface measurements for the control and HFS groups are presented in Table 2.

In ocular surface assessments, the HFS group demonstrated significantly higher OSDI scores ($p<0.001$), shorter TBUT values ($p=0.001$), reduced Schirmer's I test results ($p<0.001$), and increased corneal surface staining scores ($p<0.001$) compared to the control group. Eyelid margin abnormality scores were also significantly more severe in the HFS group ($p<0.001$). Moreover, irregular eyelid margins ($p=0.013$), vascular engorgement ($p=0.002$), plugged meibomian gland orifices ($p=0.001$), and mucocutaneous junction displacement ($p=0.033$) were all significantly more prevalent in the HFS group than in controls. The HFS group exhibited significantly greater impairment in meibomian gland function compared to controls. This was reflected in elevated meibomian gland expression scores (upper, lower, and total; all $p<0.001$), increased meibography scores (upper, lower, and total; all $p<0.001$), and more extensive gland loss areas (upper, lower, and total; all $p<0.001$).

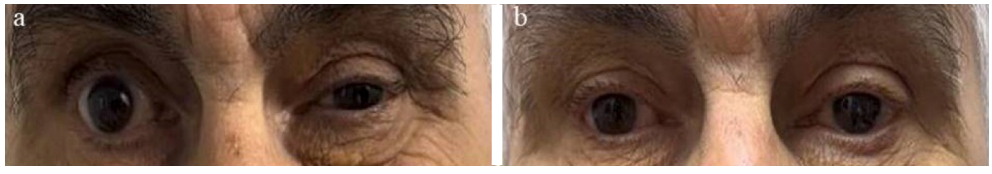

Figure 1. A patient with right-sided hemifacial spasm before **(a)** and after **(b)** botulinum toxin injections. Improved symmetry in eye opening is observed following treatment.

Table 2. Comparison of the clinical characteristics and ocular surface parameters of study groups

	Baseline			Post-BTX-A injection		
	Control (n=27)	Hemifacial spasm (n=27)	p	1 m (n=27)	3 m (n=27)	6 m (n=27)
Age (y)	62.1±10.2	62.1±10.2	1.0	62.1±10.2	62.1±10.2	62.1±10.2
Gender (Female/Male)	16/11	16/11	1.0	16/11	16/11	16/11
Body mass index (kg/m2)	26.3±3.8	26.3±3.8	1.0	26.3±3.8	26.3±3.8	26.3±3.8
Laterality (%)						
Right eye	17 (63)	10 (37)	0.057	10 (37)	10 (37)	10 (37)
Left eye	10 (37)	17 (63)		17 (63)	17 (63)	17 (63)
DED, n (%)	0 (0)	12 (44.4)	<0.001	3 (11.1)	5 (18.5)	8 (29.6)
OSDI score	15.3±8.3	27.1±12.6	<0.001	18.7±10.5	20.9±11.8	23.5±12.3
Tear break-up time (s)	9.33±5.7	5.48±3.1	0.001	8.70±5.3	7.85±4.9	6.44±4.6
Schirmer's I test (mm)	12.48±6.2	7.2±3.5	<0.001	10.5±4.9	9.63±4.6	8.7±4.3
Corneal surface staining score	1.9±1.5	7.5±3.7	<0.001	4.7±2.3	4.2±1.8	6.3±2.6
Eyelid margin abnormality score (%)	0.5±0.6	1.9±1.3	<0.001	1.1±0.8	1.3±0.9	1.6±1.1
Irregular eyelid margin	3 (11.1)	11 (40.7)	0.013	4 (14.8)	6 (22.2)	9 (33.3)
Vascular engorgement	2 (7.4)	12 (44.4)	0.002	4 (14.8)	4 (14.8)	8 (29.6)
Plugged meibomian gland orifices	3 (11.1)	14 (51.8)	0.001	3 (11.1)	5 (18.5)	11 (40.7)
Shift in the mucocutaneous junction	4 (14.8)	11 (40.7)	0.033	5 (18.5)	8 (29.6)	9 (33.3)
Meibomian expression						
Upper eyelid	0.7±0.7	1.9±1.3	<0.001	1.2±0.8	1.3±0.8	1.7±0.9
Lower eyelid	0.6±0.5	1.7±1.1	<0.001	1.0±0.9	1.1±0.9	1.6±0.9
Total	1.3±0.8	3.7±1.9	<0.001	2.2±1.5	2.5±1.6	3.3±1.8
Meibography score						
Upper eyelid	1.1±0.6	2.1±0.9	<0.001	1.4±0.8	1.5±0.8	1.7±0.8
Lower eyelid	0.9±0.5	1.9±0.9	<0.001	1.2±0.8	1.3±0.8	1.6±0.8
Total	2.1±0.9	4.1±1.2	<0.001	2.6±1.0	2.8±1.0	3.3±1.1
Area of meibomian gland loss						
Upper eyelid	17.8±7.1	40.5±19.4	<0.001	24.7±15.1	29.3±16.9	35.7±14.4
Lower eyelid	19.4±7.5	42.8±20.1	<0.001	30.3±17.1	32.4±17.9	37.6±18.1
Total	37.3±17.5	83.3±26.9	<0.001	55.1±22.3	61.7±23.4	73.3±25.9

BTX-A: Botulinum toxin A; DED: Dry eye disease; OSDI: Ocular surface disease index.

As shown in Table 3, correlation analysis was utilized to investigate the link between HFS severity and ocular surface indicators, including MGD parameters. There were significant positive correlations between the severity of HFS and several ocular surface parameters, including OSDI (r=0.506, p=0.001), corneal surface staining (r=0.537, p<0.001), meibomian gland expression (upper: r=0.543, p<0.001; lower: r=0.509, p=0.001; total: r=0.584, p<0.001), meibography scores (upper: r=0.427, p=0.016; lower: r=0.489, p=0.001; total: r=0.463, p=0.002), and the area of meibomian gland loss (upper: r=0.552, p<0.001; lower: r=0.506, p<0.001; total: r=0.538, p<0.001). In contrast, significant negative correlations were observed between HFS severity and TBUT (r=−0.454, p=0.008) as well as Schirmer's I test scores (r=−0.412, p=0.012).

A detailed comparison of ocular surface measurements and MGD in eyes with HFS at baseline and at 1, 3, and 6 months after BTX-A injection is presented in Table 4 and Figure 2. Among patients with HFS, OSDI, TBUT, Schirmer's I test, eyelid margin abnormality score, meibography scores

Table 3. The relationship between the hemifacial spasm severity and ocular surface parameters

	Hemifacial spasm severity	
	r	p
OSDI score	0.506	0.001
Tear break-up time (s)	-0.454	0.008
Schirmer's I test (mm)	-0.412	0.012
Cornea surface staining score	0.537	<0.001
Eyelid margin abnormality score	0.385	0.098
Meibomian expression		
Upper eyelid	0.543	<0.001
Lower eyelid	0.509	0.001
Total	0.584	<0.001
Meibography score		
Upper eyelid	0.427	0.016
Lower eyelid	0.489	0.001
Total	0.463	0.002
Area of meibomian gland loss		
Upper eyelid	0.552	<0.001
Lower eyelid	0.506	<0.001
Total	0.538	<0.001

OSDI: Ocular surface disease index.

(upper, lower, and total), and the extent of meibomian gland loss (upper, lower, and total) showed significant improvement at 1 ($p<0.05$) and 3 months ($p<0.05$) after BTX-A injection compared to pre-injection values. However, these improvements were no longer statistically significant 6 months after injection ($p>0.05$). Two (7.4%) eyes in our study developed a minor hematoma, which gradually resolved within 2 weeks after the injection.

Discussion

Our findings indicate a significant association between HFS and signs and symptoms of DED. A positive correlation was observed between the clinical severity of HFS and the degree of ocular surface alterations, including MGD. In addition, periocular administration of BTX-A alleviated the motor symptoms of HFS and resulted in significant improvements in ocular surface health.

In our study, the prevalence of DED among eyes affected by HFS was 44.4%. This is in line with findings by Raj et al.,(16) who reported that 8 out of 17 patients with HFS (47.06%) were diagnosed with DED, and by Pellegrini et al.,(5) who documented a prevalence of 42% (5,16). In contrast, Jariyokasol et al.(4) reported a DED prevalence of 37.93% in HFS-affected eyes, which was not statistically significantly different from that in the contralateral eyes (27.6%), despite a nearly 10% absolute difference that may be of clinical relevance (4). Differences in diagnostic criteria may explain the lower prevalence reported by Jariyokosol et al. (4) At the same time, their study employed the Asia Dry Eye Society criteria. Our study and those by Raj et al. (16) and Pellegrini et al. (5) utilized the DEWS criteria, which may be more sensitive in detecting DED.

Patients with HFS had significantly higher OSDI and corneal staining scores and significantly lower Schirmer's I test values and TBUT compared to their unaffected fellow eyes. In addition to prior research, our study presents a novel finding that eyes with HFS exhibited a higher incidence of MGD than the controls (4,5). A significant association was also observed between higher HFS severity scores and more significant impairment in subjective and objective dry eye parameters. While comparisons can be drawn between our results in HFS patients and previous findings in blepharospasm due to shared clinical characteristics, it is critical to recognize that the available literature on the effect of blepharospasm on DED lacks consistency and is marked by substantial variability (3,6,7).

Irregular and forceful blinking patterns in HFS may contribute to the pathogenesis of DED by disrupting tear film stability and reducing adequate lubrication between the ocular surfaces (17). Inadequate separation and lubrication of the eyelid and ocular surfaces can lead to repeated microtrauma during eyelid movements, particularly of the upper lid (17). This microtrauma may trigger an inflammatory cascade through the mechanism of the Lewis triple response (18). The resulting tear hyperosmolarity and mechanical stress on the epithelium may further stimulate the release of proinflammatory cytokines such as tumor necrosis factor-alpha and interleukin-1 at the ocular surface (19).

The meibomian glands are essential in preserving the homeostasis of the tear film's lipid layer, and any dysfunction may lead to increased tear evaporation and the subsequent development of DED. Our impaired meibomian gland function findings in HFS patients may be explained by morphological and functional disruptions secondary to sustained eyelid muscle spasms. Lin et al. (20) demonstrated that repetitive forced blinking and sustained spasms in blepharospasm patients were associated with reduced acinar area, lower meibum reflectivity, and increased acinar irregularity, likely reflecting diminished lipid storage. In addition, impaired Riolan muscle function may reduce gland orifice diameter, compromising lipid secretion.

Table 4. Comparison of measurements during the 6-month follow-up in the hemifacial spasm group

	Hemifacial spasm					
	Pre-injection versus			1 month versus		3 month versus
	1 month	3 month	6 month	3 month	6 month	6 month
DED, n (%)	0.006	0.040	0.259	0.443	0.091	0.339
OSDI score	0.009	0.028	0.207	0.393	0.086	0.268
Tear break-up time (s)	0.014	0.034	0.314	0.554	0.102	0.228
Schirmer's I test (mm)	0.007	0.036	0.166	0.497	0.153	0.442
Cornea surface staining score	0.002	<0.001	0.152	0.396	0.022	0.001
Eyelid margin abnormality score	0.012	0.042	0.320	0.526	0.106	0.281
Irregular eyelid margin	0.033	0.143	0.573	0.483	0.111	0.362
Vascular engorgement	0.017	0.017	0.259	1.0	0.190	0.190
Plugged meibomian gland orifices	0.001	0.010	0.412	0.443	0.013	0.074
Shift in the mucocutaneous junction	0.074	0.392	0.573	0.339	0.214	0.769
Meibomian expression						
Upper eyelid	0.004	0.015	0.464	0.476	0.006	0.027
Lower eyelid	0.001	0.010	0.326	0.344	0.004	0.032
Total	0.001	0.008	0.285	0.307	0.001	0.014
Meibography score						
Upper eyelid	0.002	0.011	0.103	0.522	0.188	0.465
Lower eyelid	0.005	0.008	0.056	0.413	0.159	0.407
Total	0.001	0.001	0.084	0.417	0.161	0.384
Area of meibomian gland loss						
Upper eyelid	0.001	0.028	0.309	0.297	0.008	0.140
Lower eyelid	<0.001	0.001	0.084	0.255	0.001	0.062
Total	<0.001	0.001	0.128	0.267	0.004	0.106

DED: Dry eye disease; OSDI: Ocular surface disease index.

The present study showed a significant improvement in OSDI scores, corneal surface staining, meibum expressibility, meibography scores, and meibomian gland loss 1 month following periocular BTX-A injection. Six months post-treatment, the observed benefits were no longer statistically significant, consistent with the temporary duration of BTX-A's neuromuscular blockade. Horwath-Winter J et al. (21) investigated the effects of standard periorbital BTX-A injections on dry eye symptoms over 3 months in patients with essential blepharospasm. According to the study, Schirmer test scores decreased significantly over time, with notable reductions recorded at 1 week, 1 month, and 3 months after the injection (21). This difference in Schirmer's results might be explained by the type of BTX-A used in their study. Specifically, abobotulinumtoxinA, known for its higher diffusion rate compared to onabotulinumtoxinA, may have caused a more widespread distribution of the toxin to the lacrimal glands, leading to a reduction in tear production as observed in the Schirmer test (22). Although Jariyakasol et al.(4) reported no statistically significant differences in tear function parameters – including basal secretion, reflex tearing, and delayed clearance – between HFS-affected and unaffected eyes based on fluorescein clearance testing, they observed higher Oxford scheme grades in the affected eyes, suggesting potential HFS-related epithelial compromise (4). BTX-A may impact tear dynamics through multiple pathways, including reduced lacrimal gland output, altered lipid layer composition, and changes in tear volume and film stability (23). These effects are likely modulated by factors such as the concentration and dose of BTX-A, the injection site, technique, and the extent of its diffusion into surrounding tissues.

Various oral medications have been investigated for managing HFS, including anticonvulsants, baclofen, anticholinergics, and haloperidol (1). However, limited reliable evidence

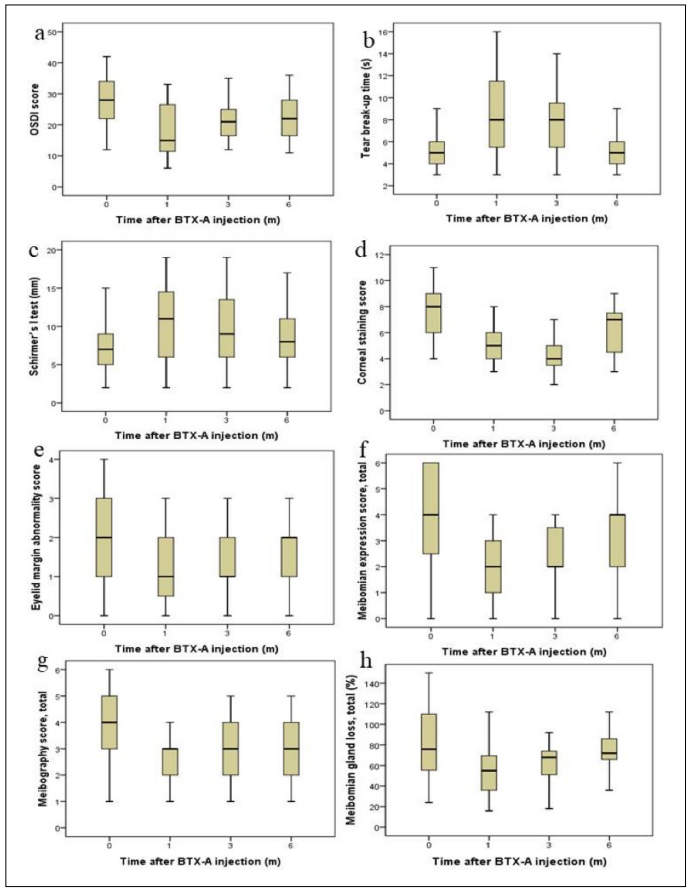

Figure 2. Ocular surface parameters before and at 1, 3, and 6 months after botulinum toxin injection: **(a)** Ocular surface disease ındex score; **(b)** tear break-up time; **(c)** Schirmer's I test; **(d)** corneal staining score; **(e)** eyelid margin abnormality score; **(f)** total meibomian gland expression score; **(g)** total meibography score; **(h)** total area of meibomian gland loss.

supports their efficacy, and treatment is often accompanied by undesirable side effects such as sedation and fatigue (1). Botulinum toxin has emerged as the most effective therapeutic intervention for HFS. The transient improvements observed in ocular surface measurements and meibomian gland function following BTX-A injections in patients with HFS may be attributed to several interconnected mechanisms. These include reducing involuntary muscle contractions, decreasing blink amplitude and frequency, prolonged ocular surface exposure, and reduced tear clearance (24). Gameiro et al. (24) demonstrated that BTX-A significantly decreased blink frequency, amplitude, and maximal eyelid closure velocity. Reduced blinking frequency may also lead to prolonged tear residence time on the ocular surface. As Sahlin et al. (25) have shown, each blink clears a measurable volume of tears, and decreased blinking may enhance tear retention, explaining the improved Schirmer's test results in our cohort. On the other hand, reports by Horwath-Winter et al.(21) and Dutton et al.(26) underscore a paradoxical reduction in tear secretion and increased ocular staining post-BTX-A, likely due to autonomic suppression of lacrimal gland function, particularly when the toxin is delivered laterally in the upper eyelid.

Our study demonstrated a favorable safety profile, with hematoma being the only complication in just 7.4% of patients. Unlike our findings, prior investigations have reported a broader range of complications, including visual disturbances, epiphora, lagophthalmos, diplopia, and ptosis (27). This relatively low complication rate may be attributed to using the pretarsal injection technique for administering BTX-A to the orbicularis oculi muscle rather than the preseptal approach. This improved performance is likely due to the functional role of the pretarsal orbicularis oculi, which is primarily responsible for involuntary blinking. In contrast, the preseptal portion facilitates voluntary, forceful eyelid closure (28,29). Furthermore, anatomical studies have shown that the pretarsal region contains more skeletal muscle fibers and greater neuronal innervation density per surface area than the preseptal region (28). The muscle fiber composition – predominantly short, type II fibers – may also promote more uniform diffusion of BTX-A across neuromuscular junctions, even at lower doses, thereby enhancing therapeutic efficiency while minimizing systemic exposure (28,30,31).

There are several limitations in this study that should be considered. The generalizability of the results to other, larger, or more diverse populations may be limited by the relatively small sample size and the single-center nature of the study. However, given the HFS's rarity, this study's sample size is relatively robust compared to previous research. Second, while using the contralateral eye as an internal control helps mitigate inter-individual variability, subtle bilateral changes or sympathetic effects may have influenced the results. Third, the cross-sectional design of the study restricts our ability to draw definitive conclusions regarding the causal relationship between HFS severity and ocular surface alterations or the long-term efficacy of BTX-A treatment. Fourth, we did not evaluate tear osmolarity, cytokine profiles, or goblet cell density, which might have provided additional mechanistic insight into the inflammatory and tear film-related changes in HFS patients. One of our study's strengths lies in using the contralateral, non-affected eyes as internal controls, which allowed for effective control of inter-individual variability and potential confounding factors. Variables known to influence dry eye, such as age, gender, race, environmental exposure, and smoking status, were inherently matched between the study and control eyes. An additional strength of the study is its focus on assessing how the clinical severity of HFS correlates with various ocular surface measures.

Conclusion

Our findings indicate that patients with HFS exhibit more severe ocular surface damage, which worsens with increasing disease severity. MGD is a contributing factor to the development of DED in this population. Our findings further suggest that BTX-A injections benefit tear film stability and meibomian gland function, offering therapeutic value beyond motor symptom relief.

Disclosures

Ethics Committee Approval: This study was approved by the Dokuz Eylul University Ethics Committee (Date:15.08.2024 Number: 2024/08-19).

Informed Consent: Written informed consent was obtained from all patients.

Conflict of Interest: None declared.

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